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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/659,326	09/11/2003	Satoshi Harashima	NANJ-0009-US1	3126

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EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	**PAPER NUMBER**
1633	

MAIL DATE	DELIVERY MODE
12/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/659,326	HARASHIMA ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 09/25/07 has been acknowledged and fully considered.

Claims 1-7 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Widianto et al (J. Fragmentation and Bio Engineering, 82(3):199-204, 1996, *ref. of record on PTO1449*) and Ascenzioni et al (PLASMID 23:16-26, 1990, *ref. of record on PTO1449*) for the reason of record as set forth in the office action mailed on 06/07/07.

Response to Argument

The applicant argues that in the conventional method, it takes a lot of time and efforts to prepare a linear chromosome splitting vector because it takes very long time to prepare a telomere sequence having many repetitive sequences. The applicant argues that the present invention can provide an efficient and easy preparation of a yeast chromosome splitting vector. The applicant argues that by using both the splitting vectors (1) and (2) simultaneously, splitting and loss of yeast chromosome become possible. The applicant furhter argues that in the present invention, it is necessary to a combined use of a linear chromosome splitting vector (1) in an order consisting of a target sequence (a), a marker gene sequence and (C_4A_2)n sequence (x) and a linear chromosome splitting vector (2) in an order consisting of a target sequence (b), a

centromere sequence of a yeast chromosome and $(C_4A_2)n$ sequence (y). The applicant argues that the prior art, Widianto (D1) and Ascenzioni (D2) fail to disclose or suggest the linear splitting vectors (1) and (2) and the combined use of the two chromosome splitting vectors.

Regarding Widianto the applicant argues that since the plasmids in the cited art are conventional vectors, therefore it takes lot of time and effort to prepare a linear chromosome splitting vector. The applicant furhter argues that Widianto does not disclose or suggest that a sequence in the linear vector of Widianto corresponds to splitting vectors (1) and (2). The applicant argues that the linear vector of Widianto contains two telomere sequences that are joined with the opposite direction to each other. The applicant argues that Widianto fails to disclose or suggest a linear vector having a target sequence at one end and telomere sequence at the other end. The applicant continues that Widianto fails to disclose or suggest the combined use of linear vectors (1) and (2) and the essentiality of combination thereof.

Regarding Ascenzioni the applicant argues that the arrangement of combination of sequences in Ascenzioni is completely different from that of the splitting vectors (1) and (2) as claimed. The applicant argues that the linear vector of Ascenzioni does not have target sequence. Ascenzioni does not disclose or suggest the sequences that correspond to the splitting vectors (1) and (2) used in the present invention. Thus, the experiment of Ascenzioni was performed merely in order to confirm the function of telomere sequence, but not for the purpose of split or loss of the chromosome. In this way, Ascenzioni fails to describe or teach splitting vectors (1) and (2). Ascenzioni fails to disclose or suggest the combined use of linear vectors (1) and (2) and the essentiality of combination thereof.

The applicant concluded that cited art Widianto and Ascenzioni fail to disclose or suggest the sequence of the linear splitting vectors (1) and (2) of the present invention. and further fail to disclose or suggest that the combined use of linear splitting vectors (1) and (2) is essential. The applicant argues that there is no motivation to combine Widianto and Ascenzioni. The applicant argues that even if the Widianto and Ascenzioni are combined, and C_4A_2 sequence is used instead of telomere sequence of Widianto,

the obtained sequence has C_4A_2 sequence at a middle portion of the chromosome and has target sequence at both ends. Therefore, it is not possible to obtain splitting vectors (1) and (2). The applicant argues that the simultaneous use of both splitting vectors (1) and (2) of the present invention would not have been obvious over Widianto and Ascenzioni and further, it would not have been obvious to even those skilled in the art to obtain a superior effects as stated above by using of both splitting vectors (1) and (2) simultaneously as claimed in the present invention.

However the applicant's arguments are found not persuasive for the reasons as set forth below:

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e. the systematic interaction of vector 1 and 2 with each other) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In instant case all what is required is the modification of yeast chromosome by a single vector which is well taught by either of the cited references of record. For example, Widianto clearly teaches a method of modifying yeast chromosome by providing a chromosome splitting vectors, wherein one of the vectors comprises centromere sequences of yeast chromosome and telomere sequences (page 200 fig 1 and 2). Similarly Ascenzioni teaches using a linear vector A241-C_4A_2 terminating at one end with the complete Tetrahymena telomere and the other with C_4A_2 oligonucleotides for the modification of yeast chromosome (page 19, co.l.2, page 25, col.1). Given the broadest reasonable interpretation invention as claimed merely requires any modification of yeast chromosome with either of one of vectors as claimed.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in

the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). The rationale to modify or combine the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art, established scientific principles, or legal precedent established by prior case law (**See MPEP 2144**).

The arguments taken as a whole rely heavily on the deficiencies of each reference taken alone. One cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In the instant case the combined teaching of cited art of record clearly suggest modification of yeast chromosome using linear vectors that contains telomere or C_4A_2 sequences with or without centromere sequences. For example Widianto clearly teaches one step splitting of chromosome by genetic transformation using vectors that contains target sequence, centromere sequence and C_4A_2 sequences (see page 200, fig 2). Similarly Ascenzioni teaches using a linear vector A241-C_4A_2 and further suggests that the presence of telomere sequences not only stabilizes the ends of linear eukaryotic chromosomes but also allows the replication (page 16, col.1 para.1). Therefore it is obvious to modify the vectors disclosed by Widianto with the teaching of Ascenzioni to produce linear vector that contains target and C_4A_2 sequences, and a vector that contains centromere and C_4A_2 sequences. One would have been motivated to do so to provide a simplified method for splitting the chromosomes in yeast cell. One would have a reasonable expectation of success, since rearrangement of genetic components for chromosomal splitting of yeast using various expression vectors has been routine in the art at time the instant invention was made and would not require "a lot of time and efforts to prepare a linear chromosome splitting vector because it takes very long time to prepare a telomere sequence having many repetitive sequences". Thus the invention as claimed is prima facie obvious in view of cited prior art of record.

Conclusion

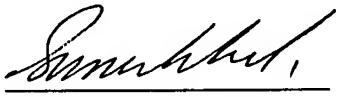
No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



SUMESH KAUSHAL
PRIMARY EXAMINER